Claims

1. A method for detecting a nucleotide mismatch in a nucleic acid sample, said method comprising the steps of:

(a) providing a nucleic acid probe derived from a hemizygous cell, said probe being complementary to a hemizygous chromosome or segment thereof present in said hemizygous cell;

(b) forming a duplex between said nucleic acid sample and said probe; and

(c) determining if said duplex contains a nucleotide mismatch.

2. The method of claim 1, wherein said determining step is carried out using a denaturing gradient gel electrophoresis technique.

3. The method of claim 1, wherein said nucleotide mismatch represents a sequence variance in a population.

4. The method of claim 1, wherein said probe has a known sequence.

5. The method of claim 1, wherein said probe is detectably labeled.

6. The method of claim 1, wherein said hemizygous cell results from the loss of a chromosome or segment thereof.

7. The method of claim 1, wherein said hemizygous cell comprises multiple copies of said hemizygous chromosome or segment thereof.

8. The method of claim 1, wherein said hemizygous cell is human.

9. The method of claim 1, wherein said hemizygous cell is an immortalized cell.

10. The method of claim 1, wherein said hemizygous cell is derived from a complete hydatidiform mole, an ovarian teratoma, an acute lymphocytic leukemia, an acute myeloid leukemia, a solid tumor, a squamous cell lung cancer, an endometrial ovarian cancer, a malignant fibrous histiocytoma, or a renal oncocytoma.

11. The method of claim 1, wherein said hemizygous cell is NALM-16 or KBM-7.

12. The method of claim 1, wherein said hemizygous cell is derived from a haploid germ cell.

13. The method of claim 1, wherein the presence of said nucleotide mismatch correlates with a level of therapeutic responsiveness to a drug or other therapeutic intervention.

14. The method of claim 1, wherein the presence of said nucleotide mismatch indicates a disease or condition, or a predisposition to develop said disease or condition.

15. The method of claim 1, wherein said nucleic acid probe is produced by amplifying at least a portion of said hemizygous chromosome or segment thereof to produce said probe.

16. The method of claim 1, wherein said determining step utilizes a protein that binds or cleaves said nucleotide mismatch.

17. The method of claim 16, wherein said protein is MutS.

18. The method of claim 16, wherein said protein is a resolvase.

19. The method of claim 18, wherein said resolvase is T4 endonuclease VII.

20. The method of claim 1, wherein said determining step utilizes a chemical agent that detects said nucleotide mismatch.

21. The method of claim 1, wherein said method is used to determine the haplotype of said nucleic acid sample.

22. A method for detecting a nucleotide mismatch in a nucleic acid sample, said method comprising the steps of:

(a) providing a nucleic acid probe derived from a sex chromosome;

(b) forming a duplex between said nucleic acid sample and said probe; and

(c) determining if said duplex contains a nucleotide mismatch.

23. A method for detecting a nucleotide mismatch in a nucleic acid sample, said method comprising the steps of:

(a) providing a nucleic acid probe derived from a somatic cell hybrid, said probe being complementary to a chromosome or segment thereof, wherein only one allele of said chromosome or segment thereof is present in said somatic cell hybrid;

(b) forming a duplex between said nucleic acid sample and said probe; and

(c) determining if said duplex contains a nucleotide mismatch.

24. A kit for detecting a nucleotide mismatch, said kit comprising:

(a) a nucleic acid probe derived from a hemizygous cell, said probe being complementary to a hemizygous chromosome or segment thereof; and

(b) a means for detecting a nucleotide mismatch.

25. The kit of claim 24, wherein said detecting means is a protein that binds or cleaves said nucleotide mismatch.

26. The kit of claim 25, wherein said protein is MutS.

27. The kit of claim 25, wherein said protein is a resolvase.

28. The kit of claim 27, wherein said resolvase is T4 endonuclease VII.

29. The kit of claim 24, wherein said detecting means is a chemical agent that detects said nucleotide mismatch.

30. The kit of claim 24, wherein said probe is detectably labeled.

31. A method for producing a nucleic acid probe for the detection of a nucleotide mismatch, said method comprising the steps of:

(a) providing a hemizygous cell having at least one hemizygous chromosome or segment thereof; and

(b) amplifying at least a portion of said hemizygous chromosome or segment thereof to produce said probe.

32. A method for producing a nucleic acid probe for the detection of a nucleotide mismatch, said method comprising the steps of:

(a) providing nucleic acid from a hemizygous cell having at least one hemizygous chromosome or segment thereof; and

(b) using said nucleic acid to produce a probe, said probe being complementary to at least a portion of said hemizygous chromosome or segment thereof.

33. The method of claim 32, wherein said nucleic acid is amplified, said amplified nucleic acid being a representation of the genomic DNA of said hemizygous cell.

34. The method of claim 32, wherein said nucleic acid is an RNA or DNA library.

35. The method of claim 31 or 32, wherein said probe has a known sequence.

36. The method of claim 31 or 32, wherein said method further comprises detectably labeling said probe.

37. The method of claim 31 or 32, wherein said hemizygous cell is human.

38. The method of claim 31 or 32, wherein said hemizygous cell is an immortalized cell.

39. The method of claim 31 or 32, wherein said hemizygous cell is derived from a complete hydatidiform mole, an ovarian teratoma, an acute lymphocytic leukemia, an acute myeloid leukemia, a solid tumor, a squamous cell lung cancer, an endometrial ovarian cancer, a malignant fibrous histiocytoma, or a renal oncocytoma.

40. The method of claim 31 or 32, wherein said hemizygous cell is NALM-16 or KBM-7.

41. The method of claim 31 or 32, wherein said hemizygous cell is derived from a haploid germ cell.

42. A nucleic acid probe for the detection of a nucleotide mismatch, said probe being derived from a hemizygous cell and being complementary to a hemizygous chromosome or segment thereof.

43. The probe of claim 42, said probe being detectably labeled.

44. A nucleic acid probe derived from an autosomal chromosome of a mammalian cell, said probe having a unique sequence.

45. The probe of claim 44, said probe being detectably labeled.